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March 24, 2008

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USPTO
Attention: Examiner Valarie Bertoglio

Serial No. 10/791,536
Docket No. 8964-0000010/US
Group Art No. 1632

This confirms that, as discussed previously by telephone, our Telephone Interview is scheduled for Monday March 31, 2008 at 10 am. Leanne M. Rakers, an associate of this firm, who has been assisting me in the present matter will also be participating in the interview.

I am attaching a DRAFT RCE, as discussed previously, incorporating an amendment and response to the outstanding action, only to facilitate our discussion. This draft will not constitute part of the formal record in this case.

Thank you for your willingness to speak with us.

Respectfully,

A handwritten signature in black ink, appearing to read "Matthew Cutler".

Matthew L. Cutler
Reg. No. 43,574
Harness, Dickey & Pierce P.L.C.

Attachment:
Draft RCE (10 pages)

MAR. 24. 2008 1:45PM

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NO. 959 P. 2

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INFORMAL COMMUNICATION; FOR DISCUSSION ONLY

NOT PART OF THE RECORD

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Application of: Lin Shiue Lian, *et al.*

Serial No.: 10/791,536

Filed: 03 March 2004

Title: METHOD OF GENERATING NEW FLUORESCENT FISH BY BREEDING TRANSGENIC FLUORESCENT FISH WITH FISH WITH DIFFERENT PHENOTYPE AND NEW FLUORESCENT FISH GENERATED THEREFROM

Group Art Unit: 1632

Examiner: Valarie E. Bertoglio

Confirmation No.: 3361

Docket No.: 8964-000010/US

Client Ref.: 0062-TK-US

Commissioner for Patents
Customer Service Window
Randolph Building
401 Dulany Street
Alexandria, VA 22314-1100

[ENTER DATE]

Sir:

REQUEST FOR CONTINUED EXAMINATION UNDER 37 C.F.R. §1.114

This paper is responsive to the final Office Action dated 11 January 2008 in which a shortened statutory period of three months was set. Applicant hereby submits a timely request for continued examination (RCE). Authorization is provided herewith to charge the fee due under 37 C.F.R. §1.17(e) to Deposit Account No. 08-0750.

AMENDMENT UNDER 37 C.F.R. §1.114 (AMENDMENT E)

Amendments IN THE CLAIMS are reflected in the listing of claims which begins on page 2 of this paper.

REMARKS on the present amendments begin on page 6 of this paper.

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IN THE CLAIMS

The following listing of claims will replace all prior versions and listings of claims in the present application.

1. (Currently Amended) A method for generating an adult oviparous teleost ornamental fish, comprising:

(a) generating a transgenic oviparous fish, wherein: the genome of the transgenic fish comprises: a transgene comprising a gene encoding a fluorescent product operably linked to α -actin or β -actin promoter and flanking ITR fragments;

(b) breeding the transgenic oviparous fish with a fish selected from the same or a different species with different phenotype or pattern to obtain transgenic progeny, wherein the transgenic oviparous fish and the fish with different phenotype or pattern are in the same genus;

(c) screening the transgenic progeny that exhibit forefins exhibiting a phenotype or pattern unlike either parent fish, and

(d) growing the transgenic progeny until adult stage.

2. (Cancelled)

3. (Cancelled)

4. (Cancelled)

5. (Previously Presented) The method as set forth in claim 1, wherein the fluorescent protein is selected from the group consisting of green fluorescent protein (GFP), modified green fluorescent protein, enhanced green fluorescent protein (EGFP), red fluorescent protein (RFP), enhanced red fluorescent protein (ERFP), blue fluorescent protein (BFP), enhanced blue fluorescent protein (EBFP), yellow fluorescent protein (YFP), enhanced yellow fluorescent protein (EYFP), cyan fluorescent protein (CFP), and enhanced cyan fluorescent protein (ECFP).

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6. (Previously Presented) The method as set forth in claim 1, wherein the fluorescent protein is selected from the group consisting of green fluorescent protein (GFP), modified green fluorescent protein, enhanced green fluorescent protein (EGFP), red fluorescent protein (RFP), enhanced red fluorescent protein (ERFP), blue fluorescent protein (BFP), enhanced blue fluorescent protein (EBFP).

7. (Previously Presented) The method as set forth in claim 1, wherein the fluorescent protein is selected from the group consisting of green fluorescent protein (GFP), modified green fluorescent protein, enhanced green fluorescent protein (EGFP), red fluorescent protein (RFP), enhanced red fluorescent protein (ERFP).

8. (Previously Presented) The method as set forth in claim 1, wherein the phenotype of the fish with different phenotype or pattern is selected from the group consisting of colors, body shapes, body sizes, body transparency, grain colors, stripe colors, fin shapes, fin sizes, tail shape, tail sizes, eye color, eye shapes, and any observable phenotypic differences from those of the transgenic fish.

9. (Previously Presented) The method as set forth in claim 1, wherein the phenotype of the fish with different phenotype or pattern is selected from the group consisting of colors, body shapes, body transparency, grain colors, and stripe colors.

10. (Previously Presented) The method as set forth in claim 1, wherein the pattern of the fish with different phenotype or pattern is selected from the group consisting of grain patterns, stripe patterns, and swimming patterns.

11-17. (Cancelled)

18. (Currently Amended) The method as set forth in claim [[16]] 27, wherein the Cyprinidae Brachydanio or Danio is selected from the group consisting of *D. acrostomus*, *D. aequipinnatus*, *D. malabaricus*, *D. albolineatus*, *D. annandalei*, *D. apogon*, *D. apopyris*, *D. assamensis*, *D. choprae*, *D. chrysotaenia*, *D. dangila*, *D. devario*, *D. fangfangae*, *D.*

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frankei, *D. fraseri*, *D. gibber*, *D. interruptus*, *D. kakhiensis*, *D. kyathit*, *D. laoensis*, *D. leptos*, *D. maetaengensis*, *D. malabaricus*, *D. naganensis*, *D. neilgherriensis*, *D. nigrofasciatus*, *D. pathirana*, *D. regina*, *D. rerio*, *D. roseus*, *D. salmonata*, *D. shanensis* *D. spinosus*, *Brachydanio frankei* [[and]] or *Branchydanio* sp.

19. (Currently Amended) The method as set forth in claim [[17]] 28, wherein the medaka is selected from the group consisting of *Oryzias javanicus*, *Oryzias latipes*, *Oryzias nigrimas*, *Oryzias luzonensis*, *Oryzias profundicola*, *Oryzias matanensis*, *Oryzias mekongensis*, *Oryzias minutillus*, *Oryzias melastigma*, *O. curvinotus*[[,]] or *O. celebensis*, ~~X. oophorus~~, and ~~X. saracae~~ *nororum*.

20. (Currently Amended) The method as set forth in claim 1, wherein the new transgenic progeny is selected from the group consisting of ~~Cichlasoma~~ TK1 red x *O. curvinotus*, TK1 green x *O. curvinotus*, TK2 red x *Brachydanio frankei*, TK2 red x *Branchydanio* sp., TK2 green x *Brachydanio frankei*, TK2 green x *Branchydanio* sp., and Purple Zebra Fish.

21. (Previously Presented) The method as set forth in claim 1, wherein the new transgenic progeny is selected from the group consisting of TK1 red x *O. curvinotus*, TK1 green x *O. curvinotus*, TK2 red x *Brachydanio frankei*, TK2 red x *Branchydanio* sp., and Purple Zebra Fish.

22. (Previously Presented) The method as set forth in claim 1, wherein the new transgenic progeny is selected from the group consisting of TK2 red x *Brachydanio frankei* and TK2 red x *Branchydanio* sp.

23. (Previously Presented) A ornamental fish which is prepared from the transgenic progeny that exhibit a phenotype or pattern unlike either parent fish selected according to the method of claim 1.

24. (Previously Presented) The fish as set forth in claim 23, wherein the fish is selected from

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the group consisting of TK1 red \times *O. curvinotus*, TK1 green \times *O. curvinotus*, TK2 red \times *Brachydanio frankei*, TK2 red \times *Branchydanio sp*, and Purple Zebra Fish.

25. (New) The method as set forth in claim 1, wherein the said genus of step (b) is a Cichlidae genus, Cyprinidae genus or medaka genus.

26. (New) The method as set forth in claim 25, wherein the Cichlidae genus is *Cichlasoma*, *Pseudotropheus*, *Pterophyllum*, *Symphysodon* or *Apistogramma*.

27. (New) The method as set forth in claim 25, wherein the Cyprinidae genus is *Cyprinus*, *Brachydanio*, *Danio* or *Carassius*.

28. (New) The method as set forth in claim 25, wherein the medaka genus is *Oryzias*.

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REMARKS

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Amendments in the claims

Following amendment as requested herein, the following claims are pending in the present application: Claims 1, 5-10 and 18-28. Claims 2, 3, 11, 16 and 17 have been cancelled herein. New Claims 25-28 have been added herein. Matter not originally filed with this specification, i.e. new matter, is not introduced by the present amendment and no change in inventorship is believed to result. Specifically:

Claim 1 is amended herein to focus on an embodiment of the invention wherein the transgenic oviparous fish is breed with a fish selected from a different species with different phenotype or pattern, and wherein the transgenic fish and the fish with different phenotype or pattern are in the same genus. This amendment is supported at least by originally filed Claims 2 and 3. Further, this amendment is made to reduce the number of issues in prosecution. No admission is made that Claim 1 as previously presented is not patentable, and Applicants may elect to reintroduce all or part of the deleted subject matter in a continuing application.

Claims 2, 3, 11, 16 and 17 are cancelled herein.

Claims 18, 19 and 20 are amended herein to coincide with the amendments made to Claim 1.

New Claims 25-28 are added herein. New Claims 25-28 are supported by Applicants' specification, at least at pages 4-5, corresponding to [0022]-[0026].

RESPONSE TO OFFICE ACTION DATED 11 JANUARY 20081. Rejection under 35 U.S.C. §112, first paragraph

Claims 1, 5-11 and 16-24 stand rejected under 35 U.S.C. §112, first paragraph, because the specification allegedly does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention commensurate in scope with these claims. Specifically, the present rejection is maintained on the grounds that the claims continue to encompass intergenus matings as well as interfamilial matings. Claims 2, 3, 11 and 16 have been cancelled, therefore the rejection as to those claims is moot. Applicants have amended Claim 1 to focus on an embodiment of the invention wherein the transgenic oviparous fish is breed with a fish selected from a different

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species with different phenotype or pattern, and wherein the transgenic fish and the fish with different phenotype or pattern are the same genus. The present rejection is now moot as this embodiment does not encompass intergenus as well as interfamily matings. Therefore, Applicants respectfully request reconsideration and withdrawal of the present rejection under 35 U.S.C. §112, first paragraph.

2. Rejection under 35 U.S.C. §112, second paragraph

Claims 1-3, 5-11 and 16-24 stand rejected under 35 U.S.C. §112, second paragraph, as allegedly indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Specifically, the phrase "screening the transgenic progeny that exhibit for those exhibiting..." is unclear. Claims 2, 3, 11 and 16 have been cancelled, therefore the rejection as to those claims is moot. Applicants have amended the phrase in Claim 1 to read "screening the transgenic progeny for those exhibiting...". Therefore, Applicants respectfully request reconsideration and withdrawal of the present rejection under 35 U.S.C. §112, second paragraph.

3. Rejection under 35 U.S.C. §102(b)

Claims 1, 2, 5-9 and 23 stand rejected under 35 U.S.C. §102(b) as allegedly anticipated by Hsiao C., *et al.* (already made of record). Claim 2 has been cancelled therefore the rejection as to that claim is moot. Further, Applicants have amended Claim 1 to focus on an embodiment of the invention wherein the breeding is performed between different species fish (interspecies). Hsiao is limited to breeding performed using the same species. Therefore, Hsiao does not teach each and every element of instant Claim 1. Applicants respectfully request reconsideration and withdrawal of the present rejection under 35 U.S.C. §102(b).

4. Rejection under 35 U.S.C. §103(a)

Claims 1, 2, 5-9 and 23 stand rejected under 35 U.S.C. §103(a) as allegedly obvious over Hsiao C., *et al.* in view of Lawson N. and Weinstein B. (already made of record). This rejection is respectfully traversed. Claim 1, as amended herein recites a method for generating an adult oviparous teleost ornamental fish, comprising, among others, breeding a transgenic oviparous fish with a fish selected from a different species with different

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phenotype or pattern to obtain transgenic progeny, wherein the transgenic fish and the fish with different phenotype or pattern are the same genus.

4.1 No motivation to combine

The Action maintains "It would have been obvious to combine the teachings of Hsiao in making a transgenic fish exhibiting stable and reproducible fluorescent reporter gene expression with those of Lawson and Weinstein to mate the transgene of Hsiao into an albino mutant fish. One of skill in the art would have been so motivated to obtain a fish exhibiting a fluorescent pattern that is not obscured by the natural pigment pattern of the fish." (present Action, page 7, lines 10-14) However, the fish species used by Hsiao is *Danio rerio*, which is the same species used in Lawson and Weinstein. If one of ordinary skill in the art were to combine Hsiao with Lawson and Weinstein (although no such motivation is admitted herein) the combination of teachings of Hsiao and teachings of Lawson and Weinstein would not lead to the presently claimed invention. Both Hsiao and Lawson and Weinstein only report intraspecies mating, as opposed to interspecies (between different species) mating. Claim 1 as amended herein, focuses on an embodiment of the invention wherein breeding is interspecies. Therefore, no motivation exists in Hsiao and Lawson and Weinstein or in the general art to arrive at the present invention.

4.2 No reasonable expectation of success

Even if motivation did exist to combine Hsiao and Lawson and Weinstein (which is not admitted herein), there is no reasonable expectation of success. "The mere fact that references can be combined or modified does not render the resultant combination obvious unless the results would have been predictable to one of ordinary skill in the art." *KSR International Co. v. Teleflex Inc.*, 127 S.Ct. 1727, 82 USPQ2d 385 (2007) (emphasis added). In this case, Applicants submit that the results were clearly unpredictable for the following reasons:

- o "Matings of distantly related species of the same genus...are highly unpredictable as to the success of the fertilization, development, health of any progeny that do occur and fertility of offspring." (see present Action, page 3, lines 9-11) Instant Claim 1 recites breeding between different species of the

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same genus.

- o "Hybridization between species often results in offspring that are sterile or with diminished reproductive capacity as a result of problems in gonad development and chromosome pairing. The results of inter-specific hybridization can lead to unexpected and undesirable results and can depend on the genetic structure of the parent fish." (see present Action, page 3, lines 12-15, citing Bartley *et al.*)
- o "While inter-specific mating of certain species is known to result in various, desirable outcomes, these combinations are not easily arrived at, as evidenced by the mating of various species of grouper [citing Bartley *et al.*]." (see present Action, page 3, lines 16-18)

Therefore, Applicant submits that one of ordinary skill in the art could not possibly have a reasonable expectation when breeding between different species as is currently recited in Claim 1.

5. Conclusion

It is believed that all of the stated grounds of rejection are properly traversed, accommodated or rendered moot herein. Applicant therefore respectfully requests that the Examiner reconsider and withdraw all presently outstanding rejections. It is believed that the present RCE is accompanied by a full and complete response to the outstanding Action and that the application is in condition for allowance.

Should any issues remain, the Examiner is invited to call the undersigned at the telephone number given below.

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Respectfully submitted,
HARNESS, DICKEY & PIERCE, P.L.C.

